

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Masaharu NODA et al.

Appl. No. NOT YET ASSIGNED

Filed: CONCURRENTLY

For:  $NA_v2$  CHANNEL GENE-  
DEFICIENT NON-HUMAN ANIMALS

Art Unit: UNKNOWN

Examiner: UNKNOWN

Atty. Docket No. 31671-173164

Customer No.



26694

PATENT TRADEMARK OFFICE

**Preliminary Amendment**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Please amend the above-identified application as follows:

**IN THE SPECIFICATION:**

Page 8, after line 14 please add the following paragraphs:

Fig. 9 is a view showing the result of the fluorescence imaging of fluorescence ratio (F340/F380) of intracellular sodium ion and extracellular calcium ion in nerve cells of dorsal root ganglia prepared from wild-type mice and Nav2 gene-deficient mice.

Fig. 10 is a view showing the result of the fluorescence imaging of fluorescence ratio (F 340/F380) of intracellular sodium ion and extracellular calcium ion in nerve cells of dorsal root ganglia prepared from wild-type mice and Nav2 gene-deficient mice.

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Fig. 11 is a view showing the result of the fluorescence imaging of fluorescence ratio (F340/F380) of intracellular sodium ion and extracellular calcium ion in nerve cells of subfornical organs prepared from wild-type mice and Nav2 gene-deficient mice.

**IN THE CLAIMS:**

Claim 13. (Amended) The fusion protein according to claim 12, wherein the protein acting as a sensor of extracellular sodium ion level is comprised of an amino acid sequence shown in Seq. ID No. 3.

Claim 15. (Amended) The antibody according to claim 14, wherein the protein acting as a sensor of extracellular sodium ion level is comprised of an amino acid sequence shown in Seq. ID No. 3.

Claim 16. (Amended) The antibody according to claim 14, wherein the antibody is a monoclonal antibody.

Claim 18. (Amended) The host cell according to claim 17, wherein the protein acting as a sensor of extracellular sodium ion level is comprised of an amino acid sequence show in Seq. ID No. 3.

Claim 20. (Amended) The transgenic non-human animal according to claim 19, wherein the protein acting as a sensor of extracellular sodium ion level is comprised of an amino acid sequence shown in Seq. ID No. 3.

Claim 21. (Amended) The transgenic non-human animal according to claim 19, wherein the non-human animal is a mouse or a rat.

Claim 23. (Amended) The method of screening a material that promotes or suppresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level according to claim 22, wherein the cell that expresses a protein acting as a sensor of extracellular sodium ion level is the host cell which contains an expression system that can express a protein acting as a sensor of extracellular sodium ion level.

Claim 24. (Amended) A method of screening a material that promotes or suppresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level characterized in using the non-human animal according to claim 1, and a subject material.

Claim 25. (Amended) A material that promotes or suppresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level characterized in being available through the screening method according to claim 22.

Claim 26. (Amended) A medical compound used for curing patients who need promotion of the function or enhancement of the expression of a protein acting as a sensor of extracellular sodium ion level, and containing the protein according to claim 9 as its effective components.

Claim 27. (Amended) A medical compound used for curing patients who need suppression of the function or the expression of a protein acting as a sensor of extracellular sodium ion level, and containing the protein according to claim 9 as its effective components.

Please add the following new claims:

Claim 28. (New) The fusion protein according to claim 12, wherein the protein acting as a sensor of extracellular sodium ion level which is comprised of amino acid sequence where one or a few amino acids are deficient, substituted, or added, in amino acid sequence shown in Seq. ID No. 3.

Claim 29. (New) The antibody according to claim 14, wherein the protein acting as a sensor of

Claim 30. (New) The host cell according to claim 17, wherein the protein acting as a sensor of extracellular sodium ion level which is comprised of amino acid sequence where one or a few amino acids are deficient, substituted, or added, in amino acid sequence shown in Seq. ID No. 3.

Claim 31. (New) The transgenic non-human animal according to claim 19, wherein the protein acting as a sensor of extracellular sodium ion level which is comprised of amino acid sequence where one or a few amino acids are deficient, substituted, or added, in amino acid sequence shown in Seq. ID No. 3.

Claim 32. (New) A method of screening a material that promotes or suppresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level characterized in using the non-human animal according to claim 19, and a subject material.

Claim 33. (New). A medical compound used for curing patients who need promotion of the function or enhancement of the expression of a protein acting as a sensor of extracellular sodium ion level, and containing the material that promotes the function or the expression of a protein acting as a sensor of extracellular sodium ion level according to claim 25 as its effective components.

Claim 34. (New) A medical compound used for curing patients who need suppression of the function or the expression of a protein acting as a sensor of extracellular sodium ion level, and containing the material that suppresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level according to claim 25 as its effective components.

Respectfully submitted,

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

Claim 13. (Amended) The fusion protein according to claim 12, wherein the protein acting as a sensor of extracellular sodium ion level is [the protein according to claims 10 or 11] comprised of an amino acid sequence shown in Seq. ID No. 3.

Claim 15. (Amended) The antibody according to claim 14, wherein the protein acting as a sensor of extracellular sodium ion level is [the protein according to claims 10 or 11] comprised of an amino acid sequence shown in Seq. ID No. 3.

Claim 16. (Amended) The antibody according to claim[s] 14 [or 15], wherein the antibody is a monoclonal antibody.

Claim 18. (Amended) The host cell according to claim 17, wherein the protein acting as a sensor of extracellular sodium ion level is [the protein according to claims 10 or 11] comprised of an amino acid sequence show in Seq. ID No. 3.

Claim 20. (Amended) The transgenic non-human animal according to claim[s] 19 [or 20], wherein the protein acting as a sensor of extracellular sodium ion level is [the protein according to claims 10 or 11] comprised of an amino acid sequence shown in Seq. ID No. 3.

Claim 21. (Amended) The transgenic non-human animal according to claim[s] 19 [or 20], wherein the non-human animal is a mouse or a rat.

Claim 23. (Amended) The method of screening a material that promotes or suppresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level according to claim 22, wherein the cell that expresses a protein acting as a sensor of extracellular sodium ion level is the host cell [according to claims 17 or 18] which contains an expression system that can express a protein acting as a sensor of extracellular sodium ion level.

Claim 24. (Amended) A method of screening a material that promotes or suppresses the function

or the expression of a protein acting as a sensor of extracellular sodium ion level characterized in using the non-human animal according to [any one of ]claim[s] 1 [to 4 or the non-human animal according to any one of claims 19 to 21],and a subject material.

Claim 25. (Amended) A material that promotes or suppresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level characterized in being available through the screening method according to [any one of] claim[s] 22[to 24].

Claim 26. (Amended) A medical compound used for curing patients who need promotion of the function or enhancement of the expression of a protein acting as a sensor of extracellular sodium ion level, and containing the protein according to [any one of ]claim[s] 9 [to 11 or the material that promotes the function or the expression of a protein acting as a sensor of extracellular sodium ion level according to claim 25] as its effective components.

Claim 27. (Amended) A medical compound used for curing patients who need suppression of the function or the expression of a protein acting as a sensor of extracellular sodium ion level, and containing the protein according to [any one of] claim[s] 9[to 11 or the material that supresses the function or the expression of a protein acting as a sensor of extracellular sodium ion level according to claim 25] as its effective components.